BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Title	:	Novel Flow Cytometer			
Inventors	:	Glenn Spaulding			
Serial No	:	09/550,276	§ Examiner	:	Gailene Gabel
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SUPPLEMENTAL APPEAL BRIEF

This Supplemental Appeal Brief is being filed in response to the Examiner's Notification of Non-Compliant Appeal Brief dated 10 April 2006. This Supplemental Appeal Brief is believed to address all the issues identified in the Examiner's Notification.

This is an appeal from the rejection of claims 1-4, 10, 11, 13-31, 33 and 34 in the Final Office Action dated 20 October 2004.

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REAL PARTY IN INTEREST

The real party in interest in the above-referenced patent application is Spin Diagnostics, Inc., a Texas corporation.

RELATED APPEALS AND INTERFERENCES

The present application was the subject of an Appeal filed 23 January 2004. In response to Appellant's prior Appeal Brief, the Examiner withdrew her Final Office Action (dated 6 October 2003) and reopened prosecution. The Examiner issued a subsequent Office Action (dated 6 May 2004) and Final Office Action (dated 20 October 2004). This appeal follows directly from this latter Final Office Action.

To the present knowledge of Appellant's representative, there are currently no related appeal or interference proceedings that will directly affect, or be directly affected by, or have a bearing on, the Board's decision in the present Appeal.

STATUS OF CLAIMS

In the Final Office Action dated 20 October 2004, claims 1-4, 10, 11, 13-31, 33 and 34 were rejected. Claims 5-9 were cancelled in response to two different restriction requirements issued by the Examiner. Claims 12 and 32 were cancelled by Appellant. Claims 1-4, 10, 11, 13-31, 33 and 34 are appealed.

STATUS OF AMENDMENTS

No amendments have been filed subsequent to the Final Office Action dated 20 October 2004.

SUMMARY OF THE CLAIMED INVENTION

Independent claims 1 and 10 are directed to "a novel flow cytometer … [in which a] … container, upon centrifugation, directs and enables the movement of cells, which have been placed in the container, towards the outer walls of the container. A light source and photodetector external to the rotating container interrogates the cells located inside of the container on the outer wall … Said apparatus and methods of interrogating said cells yield information on cell location, size, shape, cellular constituents, cell volume, and cell buoyancy; and when labeled with a fluorescent or other marker, specific cellular constituents, cell function, and genomic information … Analysis is accomplished in a sealed disposable container." (Specification at page 1, lines 7-23. See also page 3, lines 2-19. All references herein to the 'Specification' are to the substitute specification filed by Appellant on 15 August 2002 and acknowledged by the Examiner in her Office Action dated 12 November 2002.)

With respect to independent claims 1 and 10, each recites a "rotating means," a "determining means" and a "movement means." In addition, independent claim 10 recites a "detector means." (See Claims Appendix beginning at page 16.) The rotating means is identified in Figure 1 as elements 4 and 5 and in the Specification, by way of illustrative embodiments, at pages 2 (lines 15-16 and 19-21), 3 (lines 1-6), 5 (lines 8-10), 5 (line 23) to 6 (line 2) and 12 (lines 15-24). The determining means is described in the Specification by way of illustrative embodiments at pages 1 (lines 13-16), 3 (lines 28-30), 5 (line 23) to 6 (line 2), 6 (lines 28-30), 7 (lines 3-9), 9 (lines 23) to 10 (line 8) and 11 (lines 1-20). The movement means is identified in Figure 1 as elements 6, 7 and 10 and in the Specification, by way of illustrative embodiments, at pages 3 (lines 20-28), 5 (lines 13-20), 5 (line 23) to 6 (line 2) and 7 (lines 3-9 and 18-22). The detector means is identified in Figure 1 as element 8 and in the Specification, by way of illustrative embodiments, at pages 1 (lines 10-12), 2 (lines 16-19), 3 (lines 20-28), 5 (lines 10-13), 5 (line 23) to 6 (line 2), 7 (line 25) to 8 (line 6), 8 (line 21) to 9 (line 9), 9 (line 23) to 10 (line 8) and 10 (line 26) to 11 (line 20).

More generally, in the illustrative embodiment of the cytometric apparatus shown in Figure 1, a "cylinder or container having an open end and a closed end **2** has a cell guide **3** inserted into the cylinder. The cell guide has a passage through it, and is disposed in a manner such that the smaller end of the passage faces the cap **1** or other means to seal the cylinder. The larger end of the passage through the cell guide **3** opens into the cylinder **2**, both are filled with media during the process of centrifugation. The cylinder **2** is vertically rotated by a motor means **5** having a shaft **4** disposed to the cylinder in a fashion that would allow rotation around the vertical axis of cylinder **2**. A light source **9** such as an LED or laser and a photodetector **8** are adapted to interrogate cells that are dispersed to the inner surface of the wall of cylinder **2** during centrifugation. The light source **9** and photodetector **8** are disposed to a linear motion means for vertical up/down movement **6** with shaft **7** by means **10**; means **10** is adapted to precisely position the light source **9**/photodetector **8** with respect to the cylinder **2**. Said linear motion means **6** and shaft **7** is used move to the light source **9**/photodetector **8** along the vertical axis of cylinder **2**. Alternatively, the linear motion means are adapted to vertically move said rotating cylinder while the photodetectors and light sources remain in a fixed position." (Specification at page 5, lines 2-20 and Figure 1.)

Illustrative embodiments describing how the apparatus of Figure 1 may be constructed and used, including specific and enabling identification of the claimed components of the apparatus are set forth in eighteen (18) separate examples. For example, illustrative details of the claimed cylinder **2** and its associated cap **1** and cell guide **3** are discussed in examples 1 (Specification at page 5, line 22 to page 6, line 2), 2 (Specification at page 6, lines 4-12), 16 (Specification at page 11, lines 22-28) and 18 (Specification at page 12, lines 14-24). See also, page 3, lines 3-19. Similarly, illustrative details of photodetector **8** and light source **9** are described in examples 1 (Specification at page 5, line 22 to page 6, line 2), 3 (Specification at page 6, lines 14-17), 9 (Specification at page 7, line 24 to page 8, line 6), 11 (Specification at page 8, line 20 to page 9, line 9) and 15 (Specification at page 10, line 25 to page 11, line 20).

See also, page 3, lines 20-29. In addition, motion means **6** and means **10** for precisely positioning photodetector **8**/light source **9** are described in examples 1 (Specification at page 5, line 22 to page 6, line 2), 2 (Specification at page 6, lines 4-12) and 16 (Specification at page 11, lines 22-28). See also, page 3, lines 20-28 and page 4, lines 1-11. Further, illustrative analysis means are described in examples 4 (Specification at page 6, lines 19-25), 5 (Specification at page 6, lines 27-30), 12 (Specification at page 9, line 11 to page 10, line 8), 13 (Specification at page 10, lines 10-17), 14 (Specification at page 10, lines 19-23), 15 (Specification at page 10, line 25 to page 11, line 20), 17 (Specification at page 12, lines 1-12). See also, page 1, lines 17-22 and page 4, lines 1-11.

In summary, the claimed invention of independent claims 1 and 10 is directed to an apparatus that employs one or more light sources (e.g., lasers), one or more light detectors (e.g., photomultiplier tubes), mechanical motion devices (e.g., stepper motors) and analysis techniques in a manner well-known in the field of image analysis for the purpose of determining known cytometric characteristics of the media being interrogated (e.g., "size, shape, cellular constituents, cell volume, and cell buoyancy; and when labeled with a fluorescent or other marker, specific cellular constituents, cell function, and genomic information," see Specification at page 1, lines 13-16).

One of Appellant's contributions to the art is the recognition and exploitation of the fact that cytometric analysis of a sample may be performed in a closed container rotating about its longitudinal axis. No known prior art teaches, describes or fairly suggests this concept. As would be recognized by even a casual practitioner in the field of cytometric analysis in general, and flow cytometry in particular, the use of a light source and the capture of reflected and or transmitted light energy from the sample are fundamental and well understood principles that are central to the operation of any flow cytometric device.

In accordance with this recognition, noted benefits of the claimed apparatus include the elimination of a traditional flow cytometer's "complicated system of pressure

containers, valves, sheath fluid flows, orienting nozzles and other assorted equipment to move cells in single file through a gas laser light source" all of which add complexity and expense when compared to a cytometric device in accordance with the claimed invention. (Specification at page 1, lines 27 to page 2, line 8.) That is, "[c]ylinder rotation provides a novel integrated means that accomplishes cell orientation, cell localization, cell containment within a simple to manufacture and disposable container." (Specification at page 2, lines 19-21.) Another noted benefit is the claimed device's extremely high cell analysis rates (in excess of 1,000,000 cells/second) compared to the prior art flow cytometric technology. (Specification at page 4, lines 17-19.) A further benefit, one that would be understood by those in the field of flow cytometry and, in particular, those involved with the use of prior art flow cytometer devices, is the increased level of personal safety when performing cytometric analysis using the claimed apparatus – a direct result of using a closed rotating cylinder rather than an open fluid flow stream.

GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

Claim 2 stands rejected under 35 U.S.C. 112, ¶2 as being vague and indefinite for reciting "a bar code adapted to be interrogated."

Independent claims 1 and 10 and dependent claims 2, 11, 21, 22, 33 and 34 stand rejected under 35 U.S.C. 102(b) as being anticipated by US Patent 5,582,795 to Nishina et al.

Dependent claims 24, 25 and 30 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Nishina et al. in view of US Patent 5,352,879 to Milch.

Dependent claim 29 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Nishina et al. in view of US Patent 5,126,554 to Izumi.

Dependent claims 3, 13-18, 26-28 and 31 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Nishina et al. in view of US Patent 6,254,834 to Anderson et al.

Dependent claims 4, 19, 20 and 23 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Nishina et al. in view of Anderson et al. and further in view of Surmodics, Inc.

ARGUMENT

Appellant traverses the rejection contending that US Patent 5,582,795 to Nishina et al. ("Nishina") anticipates independent claims 1 and 10 and dependent claims 2, 11, 21, 22, 33 and 34 under 35 U.S.C. 102(b) in so far as Nishina does not teach or suggest all of the limitations in these claims.

Appellant further traverses the rejection contending that dependent claim 2 is vague and indefinite under section 112, ¶2 for reciting "a bar code adapted to be interrogated" in so far as it would be apparent to anyone of ordinary skill in the art what this phrase means in the context of affixing a bar code to a sample container.

With respect to the Examiner's section 103(a) rejections of dependent claims 3, 4, 13-20, 23, 26-29 and 31, Appellant relies on the patentability of independent claims 1 and 10 for their validity.

Nishina Fails to Disclose or Even Suggest Determining a Cytometric Characteristic of a Sample Disposed in a Transparent Cylinder

In rejecting independent claims 1 and 10 and dependent claims 2, 11, 21, 22, 33 and 34, the Final Office Action contends that Nishina discloses an "apparatus for use in analyzing fluids such as blood and medicines (see column 1, lines 6-9)." (Final Office Action, dated 20 October 2004, at page 6.)

"For a prior art reference to anticipate in terms of 35 U.S.C. 102, every element of the claimed invention must be identically shown in a single reference." *Diversitech Corp. v. Century Steps, Inc.*, 850 F.2d 675, 677, 7 U.S.P.Q.2d 1315, 1317 (Fed. Cir. 1988). Further, the "identical invention must be shown in as complete detail as is contained in the patent claim" (*Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 U.S.P.Q.2d 1913, 1920 (Fed. Cir.), *cert. denied*, 493 U.S. 853 (1989)), and the "elements must be arranged as in the claim under review" (*In re Bond*, 910 F.2d 831, 832, 15 U.S.P.Q.2d 1566, 1567 (Fed. Cir. 1990), *reh'g denied*, 1990 U.S. App. LEXIS 19971 (Fed. Cir. 1990)). *See also* M.P.E.P. 2131. Therefore, for Nishina to anticipate

independent claims 1 and 10 and dependent claims 2, 11, 21, 22, 33 and 34, Nishina must disclose each element contained in the claims, and there must be no difference between the claimed invention and the disclosure of Nishina. Nishina does not meet this burden.

Nishina is directed "to a hold-transfer system for extraction containers which are used for analyzing liquids such as blood and medicines in the medical field." (Nishina at col. 1, lines 6-8.) Systems in accordance with Nishina comprise "a main body and cassette … The cassette comprises holding means for holding extraction containers in an upright position, an endless travelling [sic] unit … [and] a driving rotor and driven rotor … so that the endless travelling [sic] unit can travel." (Nishina at col. 1, line 60 to col. 2, line 3; see also col. 2, lines 10-26.) In accordance with Nishina, extraction containers are affixed to a chain 16 (via metal fittings 17) which is rotated along an oblong path by sprockets 14 and 15 in conjunction with motor 27, timing pulleys 24 and 25, timing belt 26 and shafts 22 and 23. (Nishina at col. 3, lines 4-38 and FIG. 1.) Nishina also teaches that this transport may be periodically stopped and an individual extraction container rotated so that bar code reader 33 can read a bar code affixed thereto. (Nishina at col. 5, lines 4-20 and FIG. 2.) Once the bar code is read, Nishina teaches that a pipette nozzle can be lowered into the container and a sample extracted there from – hence Nishina's use of the term "extraction containers." (Nishina at col. 2, line 65 to col. 3, line 1; col. 3, lines 50-54, element 35 in FIGS. 1 and 2; col. 4, lines 17-19; col. 4, line 67 to col. 5, line 3; col. 5, lines 22-33.) Once samples from all of the containers are extracted, the cassette holding the containers is removed and a new cassette with new containers is inserted so that fluids may be extracted from them. (Nishina at col. 5, lines 34-37.)

Nowhere does Nishina teach that his apparatus be used to determine a cytometric characteristic of the liquid *within* his extraction containers. In fact, Nishina teaches that samples are *extracted* from his containers for analysis. Thus, not only does Nishina not teach the recited "*determining at least one cytometric characteristic of a*

sample disposed in said transparent cylinder," ***Nishina teaches away*** from this element because Nishina teaches extracting samples from his containers for analysis. Further, Nishina distinguishes the use of a bar code to determine the location of an extraction container (see discussion above) from the analysis of the extracted sample. Accordingly, Nishina itself refutes the Examiner's attempted interpretation with respect to her section 102 rejection.

Appellant further submits that the distinction between reading a bar code affixed to a container and determining a cytometric characteristic of a sample disposed in a container would be clear to one of ordinary skill in the art, but is also made absolutely clear by virtue of pending dependent claim 2. Dependent claim 2 recites a container further comprising "a bar code label affixed to an outer wall thereof, said bar code label adapted to be interrogated by said detector means." For dependent claim 2 to have any significance, the act of reading a bar code must be different from the act of determining a cytometric characteristic as recited in independent claim 1. Ergo, reading a bar code *is not* the same as determining a cytometric characteristic.

For at least the reasons discussed here, Nishina cannot legally anticipate the inventions of independent claims 1 and 10. Because claims 2, 11, 21, 22, 33 and 34 depend from one of independent claims 1 and 10, these claims too are not anticipated by Nishina.

The Claim Language "Bar Code Adapted To Be Interrogated" is not Vague and Indefinite

The Final Office Action contends that use of the phrase "a bar code adapted to be interrogated" is vague and indefinite because it is unclear how the barcode has been modified, i.e., adapted, so as to be interrogated. (Final Office Action at page 2.)

Bar codes are in such wide use in industry (not just the medical diagnostic field) that Appellant does not comprehend the Examiner's uncertainty. One obvious and logical interpretation of the "adapted" language of claim 2 is that the label is placed on

the recited transparent cylinder so that the bar code faces "outward" toward the detector. Another obvious adaptation is that the bar code is oriented properly for the detector (if necessary). It is further noted that the Examiner did not seem to have any trouble understanding what this phrase meant in the context of Nishina, a reference that clearly uses a bar code in the same manner as recited in dependent claim 2.

For at least these reasons, and those cited above with respect to independent claims 1 and 10 in the context of Nishina, dependent claim 2 is not vague and indefinite in the context of the described invention and, especially, as depending from independent claim 1.

Dependent Claims 3, 4, 13-20 and 23-31 are not Obvious in light of the Cited Prior Art

Each claim rejected under 35 U.S.C. 103(a) depends from one of independent claims 1 and 10. For at least the reasons set forth above, independent claims 1 and 10 are patentable over the cited prior art. Since it is axiomatic that each claim depending from a patentable claim is itself patentable, claims 3, 4, 13-20 and 23-31 are patentable over the cited prior art.

CONCLUSIONS

Nishina does not teach or suggest all of the limitations recited in Appellant's independent claims 1 and 10 for at least two reasons: (1) Nishina teaches that samples are extracted from the containers for analysis – a teaching directly contrary to the claimed limitation; and (2) Nishina teaches the use of a bar code only to determine the location of a sample container and not for purposes of analysis (determining a cytometric characteristic). Therefore, Nishina cannot anticipate claims 1, 2, 10, 11, 21, 22, 33 and 34. Accordingly, Appellant respectfully requests that the Board grant Appellant's appeal and withdraw the rejection of claims 1, 2, 10, 11, 21, 22, 33 and 34 under 35 U.S.C. 102(b) to Nishina.

Because each of claims 3, 4, 13-20, 23, 26-29 and 31 depends from one of independent claims 1 and 10 and these claims are not anticipated as described above, Appellant respectfully requests that the Board grant Appellant's appeal and withdraw the rejection of claims 3, 4, 13-20, 23, 26-29 and 31 under 35 U.S.C. 103(a).

Because use of the phrase "a bar code adapted to be interrogated" is not vague and indefinite in the context of the claimed invention, Appellant respectfully requests that the Board grant Appellant's appeal and withdraw the rejection of claim 2 under 35 U.S.C. 112, ¶2.

Respectfully submitted,

April 20, 2006
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CLAIMS APPENDIX

1. (Previously Presented) A cytometer apparatus comprising:

a rotating means adapted to receive and rotate a transparent cylinder along a longitudinal axis of the transparent cylinder;

a light source for illuminating at least a portion of said transparent cylinder while the transparent cylinder is being rotated by the rotating means;

a detector for detecting a light signal provided by said light source and reflected from said transparent cylinder while the transparent cylinder is being rotated by the rotating means;

determining means for determining at least one cytometric characteristic of a sample disposed in said transparent cylinder based on said light signal; and

a movement means for moving said transparent cylinder and said light source and detector in a longitudinal axis relative to one another.

2. (Previously Presented) The cytometer apparatus as set forth in claim 1, wherein said transparent cylinder comprises a bar code label affixed to an outer wall thereof, said bar code label adapted to be interrogated by said detector means.

3. (Previously Presented) The cytometer apparatus as set forth in claim 1, wherein said transparent cylinder has an inner wall having calibration standards affixed thereon.

4. (Previously Presented) The cytometer apparatus as set forth in claim 1, wherein said transparent cylinder comprises an inner wall having a photoactivated crosslinker affixed thereon.

10. (Previously Presented) A spin cytometer, comprising:

a rotating means for rotating a transparent cylinder about a longitudinal axis of the transparent cylinder;

a light source for illuminating at least a portion of the transparent cylinder while the transparent cylinder is being rotated by the rotating means;

a detector means for detecting a light signal generated by the light source and reflected from the transparent cylinder while the transparent cylinder is being rotated by the rotating means;

determining means for determining at least one cytometric characteristic of a sample disposed in said transparent cylinder based on said detected light signal; and

a movement means for moving the transparent cylinder and the light source and detector means in relative motion.

11. (Previously Presented) The spin cytometer of claim 10, wherein the rotating means is adapted to sequentially rotate a transparent cylinder in two (2) directions.

13. (Previously Presented) The spin cytometer of claim 10, wherein the rotating means is adapted to rotate a transparent cylinder comprising:

a closed end;

an open end;

a cell guide member having a first side oriented toward the open end, a second side oriented toward the closed end, and a passage from the first side to the second side; and

a cap for sealing the open end.

14. (Previously Presented) The spin cytometer of claim 13, wherein the passage is smaller at said first side than it is at said second side.

15. (Previously Presented) The spin cytometer of claim 14, wherein the passage is substantially smaller than the diameter of said transparent cylinder.

16. (Previously Presented) The spin cytometer of claim 13, wherein the closed end has a smaller outside diameter than the open end.

17. (Previously Presented) The spin cytometer of claim 13, wherein said transparent cylinder comprises a polystyrene cylinder.

18. The spin cytometer of claim 13, wherein an inner wall of said transparent cylinder comprises an organic photoreceptor material affixed thereon.

19. (Previously Presented) The spin cytometer of claim 18, wherein the organic photoreceptor material is activated by a wave length of approximately 300 nanometers to approximately 800 nanometers.

20. (Previously Presented) The spin cytometer of claim 19, wherein the organic photoreceptor material comprises dibromo anthanthrone.

21. (Previously Presented) The spin cytometer of claim 10, wherein the rotating means comprises a stepper motor.

22. (Previously Presented) The spin cytometer of claim 10, wherein the light source comprises a light emitting diode.

23. (Previously Presented) The spin cytometer of claim 22, wherein the light emitting diode is adapted to emit a light having a wavelength of between approximately 300 nanometers and 800 nanometers.

24. (Previously Presented) The spin cytometer of claim 10, wherein the detector means further comprises an analog to digital converter.

25. (Previously Presented) The spin cytometer of claim 24, wherein the detector means further comprises a processing means for associating a location identifier with an analog to digital converter output value, the location identifier identifying a location on a surface of the transparent cylinder at which the digital to analog value was obtained.

26. (Previously Presented) The spin cytometer of claim 10, further comprising an additional one (1) or more light sources, each light source adapted to illuminate at least a portion of the transparent cylinder.

27. (Previously Presented) The spin cytometer of claim 26, wherein each of the additional one (1) or more light sources are adapted to emit a different wavelength.

28. (Previously Presented) The spin cytometer of claim 10, further comprising at least one diffraction grating.

29. (Previously Presented) The spin cytometer of claim 10, wherein the detector means comprises a photomultiplier.

30. (Previously Presented) The spin cytometer of claim 10, wherein the detector means comprises a charge coupled device.

31. (Previously Presented) The spin cytometer of claim 27, further comprising an additional one (1) or more detector means, each detector means responsive to a light signal generated by one of the light sources.

33. (Previously Presented) The spin cytometer of claim 10, wherein the movement means moves the transparent cylinder in a direction substantially parallel to the transparent cylinder's longitudinal axis.

34. (Previously Presented) The spin cytometer of claim 10, wherein the movement means moves the light source and detector means in a direction substantially parallel to the transparent cylinder's longitudinal axis.

EVIDENCE APPENDIX

<<NONE>>